

WHAT IS CLAIMED IS:

1. A method of treating an individual having a pathophysiological state, comprising the steps of:

5 a). administering to said individual a pharmacologically effective dose of a agent which up-regulates the expression of a cellular target; and,

mb  
8  
b) administering to the same individual a pharmacologically effective dose of an immunotoxin directed against  
10 the up-regulated cellular target.

662070:040700  
2. The method of claim 1, wherein the administered agent is selected from the group consisting of differentiating agents,  
15 cytokines, interleukin-2, tumor necrosis factor, interferon- $\alpha$ , interferon- $\gamma$  and peptide hormones.

3. The method of claim 1, wherein said agent is a  
20 retinoid and wherein said cell target is the CD38 antigen.

4. The method of claim 3, wherein said pathophysiological state is selected from the group consisting of acute myeloid leukemia, acute promyelocytic leukemia, lymphomas, and myelomas.

5. The method of claim 3, wherein said retinoid is selected from the group consisting of all-*trans*-retinoic acid (RA); 9-*cis* retinoic acid (9-*cis* RA); (*E*)-4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-1-propenyl]benzoic acid (TTNPB); (*E*)-4-[2-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-1-propenyl]benzoic acid (3-met TTNPB).

15

6. The method of claim 5, wherein said retinoid is administered in a dose of from about 0.1 mg/kg to about 2 mg/kg.

7. The method of claim 3, wherein said immunotoxin specifically targets cells expressing the CD38 antigen.

8. The method of claim 7, wherein said immunotoxin comprises a monoclonal antibody directed against the CD38 antigen conjugated to a toxin molecule.

5

9. The method of claim 8, wherein said toxin is gelonin.

10

10. The method of claim 8, wherein the monoclonal antibody is selected from the group consisting of IB4 or IB6.

15

11. The method of claim 1, wherein said immunotoxin is administered in a dose of from about 0.05 mg/kg to about 2 mg/kg.